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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/975,300	10/12/2001	Dan Canaani	P-4393-US1	8148

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EXAMINER	
PONNALURI, PADMASHRI	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 02/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/975,300	CANAANI ET AL.	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-88* is/are pending in the application.

4a) Of the above claim(s) *10-83 and 86-88* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9, 84 and 85* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/21/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group I, claims 1-9, 84-85 in Paper No. 11052003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 10-83, 86-88 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 11052003.

3. Claims 1-8, 84-85 are currently being examined in this application.

4. This application is a continuation-in-part of application 09/391,444 filed on 08 September 1999.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-9, 84-85 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claims briefly recite a method for screening molecule, which has a synthetic

lethal property in mammalian cells.

The specification disclosure is drawn to the use of specific Epstein-Barr virus based episomal vectors in the claimed method. The specification discloses that the episomal vectors have to replicate autonomously in mammalian cells and retained by the cells. The specification discloses the use of GSE containing episomes in the claimed method. The specification examples are drawn to use of specific Epstein-barr virus based vectors. The specification disclosure is directed to the use of specific Epstein-barr virus based vectors, which clearly does not provide adequate support regarding the open ended method of using a surival palsmid to screen synthetic lethal property in mammalian cells.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

Thus, it requires a representative sample of compounds and/or a showing of sufficient identifying characteristics; to demonstrate possession of the claimed generic(s).

In the present instance, the claimed invention contains no identifying characteristics regarding the vectors other than the Epstein-barr virus based vectors in the claimed method.

Additionally, the examples in the specification drawn to specific vectors is clearly not representative of the presently claimed invention.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-9, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites in step VIII, 'removing selection for the selectable marker.'. It is not clear what does applicants mean by removing the selection for selectable marker', does applicants mean 'stopping the selection for the selectable marker' or the selectable marker is removed from the cells and molecules to be screened are added. Applicants are requested to amend the claim to clear the ambiguity.

Claim 1 recites in line 1, 'molecule which have a synthetic lethal property', which needs to be corrected as 'molecule which has a synthetic lethal property.'

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: The claimed method recites a method for screening molecule, however the claimed method does not recite whether the molecule to be screened is transfected into a vector. The instant claimed method recites that the molecules are added to the survival plasmids selected in step vii. And further the method seems to be missing a method step 'how a molecule having a synthetic lethal property is identified by determining the survival plasmid.

What is the relationship between the survival plasmid determination in step ix and molecule to be screened. Applicants are requested to amend the claim. .

Claim 5 recites the limitation "the products of said first and second reporter genes". There is insufficient antecedent basis for this limitation in the claim or in claim 1.

Claim 5 recites the limitation "said first and second reporter genes" . There is insufficient antecedent basis for this limitation in the claim or in claim 1.

Claim 7 recites the limitation "said human cells". There is insufficient antecedent basis for this limitation in the claim or in claim 1.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-9 and 84-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deiss et al (Science, vol. 252, pages 117-120, April 1991) and Wade-Martins et al (Nucleic acid Research, vol. 27, number 7, pages 1674-1682, 1999).

Deiss et al teach a genetic method to identify thioredoxin as a mediator of growth inhibitory signal. The reference teaches Technical knock out (TKO) selection method based on the random inactivation of genes via cDNA library cloned into anti-sense expression vector. The reference uses a Epstein-Barr virus (EBV) episomal vector to transduce the cDNA library because it efficiently transfects human cells. The episomal vector contains the Epstein-Barr virus nuclear antigen type I coding sequence (EBNA-1), the ori P (the episomal origin of replication, a Hygromycin B resistance marker. The cDNA was inserted into the vector in the anti-sense orientation, and the EBV vectors with the library are introduced into the HeLa cells. The cells were selected with Hygromycin B to determine the transfection. The transfected cells are selected with Hygromycin B and IFN-γ. The cells with antisense libraries have survived, and the anti-sense vectors contained cells were isolated by the method of Hirt, and the cDNA insert contained in the vector was subcloned and the sequence found match to that of human thioredoxin. The reference also teaches that anti-thioredoxin vector (pTKO1-ATx) was introduced into HeLa cells, and pools of Hygromycin B resistant cells were generated. The pools of cells then cultured in the presence of both Hygromycin B and IFN-γ. The presence of pTKO1-ATx significantly decreased sensitivity of transfected cells to growth inhibition. This is reflected by increase in the number of colonies growing in presence of IFN-γ. The reference teaches the HeLa cells have thioredoxin. The reference teaches that TKO selection method can be used to identify genes, and tumor suppressor genes.

The claimed invention differs from the prior art teachings by using reporter genes in the vector. Deiss et al do not teach the use of reporter gene. However, Wade-Martins et al teach episomal shuttle vectors in human cells. The reference teaches episomal vectors which can transfer large human genomic DNA inserts. The episome/vector has FR region (equal to oriP), EBV nuclear antigen 1 (for nuclear retention), Hygromycin-B phosphotransferase (HPH, the marker) and enhanced green fluorescent protein gene (GFP) as reporter (see i.e., figure 1). The presence of GFP offers the advantage of being able to track the episomes in live cells. The reference teaches that a series of ell-characterized genomic DNA inserts from PAC library are cloned in the vectors. The vectors carrying the large inserts were shown episomally in a manner comparable with small EBV oriP vectors. The vectors are transfected into MRC5 cells (human fibroblast cell line) and selected using HPH, and individual colonies which are selected are grown in HPH. The HPH-resistant colonies, which also express GFP are picked, which has the gene of interest. The reference teaches that the disclosed vectors are good candidates for gene expression studies and in gene therapy protocols and the GFP allows to track the presence of episomes in live cells. Thus, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use GFP protein in the expression vectors of Deiss et al, because Wade-Martins et al teach that GFP allows to track the presence of episomes in live cells. The person skilled in the art would have been motivated to use the method of screening a cDNA library taught by Deiss et al with the GFP protein gene as reporter gene, because GFP allows to track the vectors in live cells and Deiss et al teach that the method can be used to identify tumor suppressor genes. Claims 84-85 have been included in this rejection because a person skilled in the art would have been motivated to collect all the reagents useful in the method for screening a

chemical library as taught by Deiss et al and Wade-Martins et al and dispense the reagents in a kit for ease of use.

Conclusion

No claims are allowed.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicants cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner is on Flex schedule and can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

Pp
February 09, 2004.